International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Issue 6, 2022

Original Article

PREPARATION OF SALBUTAMOL SULPHATE LOADED LOCUST BEAN GUM-POLYVINYL ALCOHOL COMPOSITE CRYOGEL FOR DRUG DELIVERY

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Received: 01 Apr 2022, Revised and Accepted: 22 Sep 2022

ABSTRACT

Objective: The key goal of the experimental study involves the preparation of salbutamol sulphate drug-loaded freeze thawed composite cryogels, comprising locust bean gum and polyvinyl alcohol and evaluating them for drug delivery.

Methods: The cryogels were formulated using freeze thaw process and characterization was performed using numerous techniques like Fourier transform-infrared spectroscopy, differential scanning calorimetry, scanning electron microscopy, X-ray diffraction studies, swelling behaviour and *in vitro* drug release.

Results: FTIR spectra of drug loaded LBG-PVA composite cryogels showed sharp peak at 3437 cm^{-1} owing to O-H stretching of free hydroxyl groups. DSC thermogram of LBG-PVA composite cryogels displayed a broad endotherm with hump at 190.85 °C. XRD analysis of LBG-PVA composite cryogel indicated characteristic peak at 19.83° (2θ) which suggest that formation of cryogels between two polymers contributes to a decrease in crystallinity. SEM analysis depicted that LBG-PVA composite cryogels were porous in nature as interconnected and irregular pores with thick walls. Swelling study inferred that on increasing the concentration of both polymers the swelling ability of LBG-PVA increased considerably. Results obtained from optimization study suggested that greater concentration of both locust bean gum and polyvinyl alcohol favoured release of salbutamol sulphate in a sustained manner. The experimental findings display *in vitro* release of salbutamol sulphate as 77.75% over duration of 24 h following Higuchi's square root release kinetics.

Conclusion: The outcomes of the experimental investigation depicted that locust bean gum in combination with polyvinyl alcohol favoured synergistically with release of salbutamol sulphate in a sustained manner.

Keywords: Cryogel, Drug delivery, Freeze thaw process, Locust bean gum, Polymer modification, Sustained release

DOI: https://dx.doi.org/10.22159/ijap.2022v14i6.44816. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Polymer generally has high molecular weight that varies between (10,000-10, 00,000 g/mol) and constitutes numerous structural units bonded via covalent bonds [1]. Polymers or macromolecules obtained from both, natural and synthetic sources are mainly used for fabrication of different formulations for further usage in drug delivery systems [2]. Recently, demand has grown for use of natural polymers due to their cost effectiveness and biodegradability. Natural originated polymers possess wide-ranging applications in the medicinal field as well as in the food industry as thickening [3], bio adhesive [4], gelling [5], binding [6] and film forming agents [7], and also as agents for altering release rate [8]. The primary advantages associated with polymers of natural origin are their accessibility, low-priced, biodegradability, and biologically compatible nature. To modify the polymer properties, a number of physical and chemical approaches were used [9]. Various methods used for chemical modification includes carboxymethylation [10], grafting [11], cross linking [12], thiolation [13], carbonylation [14], and propylation [15]. One of the promising methods used to physically alter the properties of natural polymers is freeze-thaw process. In freeze-thaw process, the formulation is freeze at (-5 to-20) °C and then thawed at room temperature. This physical modification approach alters polymer properties with no effect on the toxicity profile, so these approaches are favoured over other approaches [16]. This method supports the cross linking between polymer chains without the use of chemical agents. At the higher sub-zero temperature (around-20 °C), the solvent freezing rate is slow, which results in the formation of irregular and random ice crystals besides larger pore size [17, 18].

Locust bean gum is a carob seed-derived polymer, which is botanically named as *Ceratonia siliqua*, belongs to family *Leguminosae* and comprised of mannose and galactose units and, hence, comes under class of galactomannans. It is a powder having white to creamy white colour [19]. The various discrete functions of locust bean gum make it, a polymer of choice in biopharmaceutical applications, from excipient employed in controlled release preparations to disintegrant used in formation of tablets [20]. Locust bean gum has excellent ability of forming gel and shows better interactions with different polymers due to presence of several OH groups in its molecular structure, so an escalating importance is being noticed about its use in area of biopharmaceutics. Also, itis now employed for preparation of numerous dosage forms like nanoparticles, tablets (matrix formation) and gels [21].

Cryogels are referred as hydrogels prepared at sub-zero temperature (below 0 °C) and yields distinct properties intended for discrete bioengineering and biotechnological applications [22]. A system containing large interconnected pores is the fundamental characteristic feature of cryogels. The size of the macropores inside the cryogels ranges from 10 to 100 µm. It displays greater tensile strength besides higher elasticity as compared to hydrogels which are cross linked through many chemical agents [23]. Cryogels, as macroporous material, are attractive as matrices for tissue scaffolding, as they facilitate diffusion of not only low-molecular weight solutes, but also, of macromolecules and cells. Mainly, cryogel formation occur in a freezing condition in which chemical reaction leads to gelationat temperature between (-5 to-20) °C at which major portion of the solvent crystallizes [24]. When freezing process completes at required duration of time, then thawing process is conducted at conditions of room temperature for melting the ice crystals and, leaving behind the interconnected and, micro porous structure [25, 26]. Numerous experimental works has been conducted for cryogel preparation using variety of polymers that

consist of carboxymethyl curdlan [27], hyaluronic acid [28], maltodextrins [29], xanthan gum [30] and locust bean gum [31]. Cryogels that are fabricated by blending synthetic polymers and polymers of natural origin have come out as promising materials for fabrication of new macro porous architectures that have novel applications in the area of biomedicines and biotechnology [32]. A wide variety of cryogels are prepared using synthetic polymer such as polyvinyl alcohol [33]. Polyvinyl alcohol (PVA) is a polymer of synthetic origin (obtained by hydrolysis of polyvinyl acetate) and is biologically compatible, non-toxic, biodegradable as well as outstanding film making polymer [34]. PVA has capability of cross linking with other cross-linking agents. Many polysaccharides have been combined with PVA to form composite cryogels that covers sodium alginate [35], chitosan [36], dextran [37] and carboxymethylcellulose [38]. Moreover, polymer blending of natural and synthetic polymers is considered more favourable as it is used to overcome the reduced biological performance of drug along with improvement in mechanical strength [39].

In the current experimental study, salbutamol sulphate loaded composite cryogels using locust bean gum and polyvinyl alcohol were formulated where salbutamol sulphateie anti-asthmatic drug was taken as model drug. The optimized batch was further evaluated using various techniques such as fouriertrans form-infrared spectroscopy, differential scanning calorimetry, X-ray diffraction and scanning electron microscopy etc.

MATERIALS AND METHODS

Materials

Locust beangum (LBG) was brought from Hi-media Laboratories Pvt. Ltd (Nashik India). Polyvinyl alcohol (average M_w=1, 25,000 g/mol, degree of polymerization=2800) was purchased from Thomas baker Chemicals Pvt. Ltd. (Mumbai, India). Salbutamol sulphate incorporated as model drug, was gift sample obtained from Orex Pharma Pvt. Ltd (Thane, Maharashtra, India). The freeze thaw method was employed for formation of locust bean gum and polyvinyl alcohol composite cryogels [9].

Formulation of LBG-PVA composite cryogel

The composite cryogel of LBG and PVA were formulated using freeze thaw process [9]. Both polymers i.e., LBG and PVA were dispersed in hot water separately at 85 °C for 20 min until solid content was no longer visible and clear solution was formed. Then, both polymers were mixed under sonication for 5 min to prepare homogenous and free of air bubbles dispersion as per design protocol (table 1). Further, this mixture was transferred in petri dishes and kept for freezing at-20 °C for 20 h and for thawing at room temperature for 4 h by three consecutive cycles upto 72hto prepare cryogels [9, 40]. For preparing the compositecryogel, drying was carried out in a lyophilizer (Alpha 2-4LD, Martin Christ, Germany) at-80 °C in the presence of pressure (0.0010 m Bar) for duration of 24 h. Finally, after completing freeze and thaw procedure, the immersion of cryogels in deionised water was done for removing the unreacted residue.

For preparing salbutamol sulphate loaded composite cryogels, the powder obtained from lyophilized cryogel (1g) was soaked in salbutamol sulphate 0.1 (%, w/v) solution and subjected to swelling for duration of 1 h at conditions of room temperature, although the absolute amount of salbutamol sulphate solution was uptakenviacryogel matrices. Then, salbutamol sulphate incorporatedcryogel matrices were dried out using lyophilizer (Alpha 2-Martin Christ, Germany) at-80 °C for duration of 24 h.

Experimental design

Optimization of composite cryogels comprising of LBG-PVA was executed using two factor-three level factorial design. The independent variables were LBG and PVA in numerous concentrations, while swelling index and *in vitro* drug release of drug through cryogels were chosen as the response variable, based on preliminary experiments. Influence of variables on the response were analysed in ranges that are three in number, i.e.-1(low), 0(middle) and+1 (high). Data was statistically analysed by employing the Design Expert software (Version 10.0, Stat EaseInc. Minneapolis, MN).

Characterization

Fourier transform-infrared spectroscopy (FTIR)

FTIR is a versatile technique used for the analysis of polymers, drug and final formulation. The spectrometer (IR, affinity, DRS-8000A, Shimadzu, Japan) was used for the analysis of functional group present in the samples using diffuse reflectance method. In this technique, before starting the process, samples were thoroughly dehydrated, in order to fully eliminate the moisture however the compressed disc preparation is not needed in the diffuse reflectance method. Therefore, dried samples were carefully mixed in very small amount of dried potassium bromide and then placed in the sample stub having shape of cup for detecting the structure and functional groups. Infrared region with a scale of 4000–400 cm^{-1} was analysed further using which spectra were obtained between the X-axis i.e., wave number (cm^{-1}) and Y-axis i.e., transmittance (%).

Differential scanning calorimetry (DSC)

Differential scanning calorimetric analysis was done for studying thermal behaviour and performed using diffraction scanning calorimeter (Perkin-Elmer, USA). Sealing of samples was done by placing the samples in aluminium pan in addition to heating in the range of (30-300) °C with the rate of heating 10 °C/min in nitrogen atmosphere.

X-ray diffraction measurements (XRD)

X-ray diffraction is an analytical technique used to measure crystallinity and phase conformation (purity) of the samples. The LBG-PVA compositecryogel sample was scanned by means of X-ray diffract meter (PAN Analytical, Almelo) from 0°-80° diffraction angle (2θ) range under the mentioned conditions: source, nickel filtered CU-Kα radiation; voltage 35KV; current 25mA; scan speed0.05 min^{-1}, division slit 1.25° and receiving slit 0.3 nm.

Scanning electron microscopy (SEM)

For detecting the morphology of LBG-PVA composite cryogels, scanning electron microscope (FEI APREO S) was used. Sample used in analysis was coated with gold for the 40s by setting on sample stub by means of double-sided adhesive tape of carbon. Coating process was carried out in presence of argon gas. Gold coating was done via Sputter coater (Quorum-Q150 TES).

Percentage of swelling

Swelling test of optimized batch of composite cryogel was conducted in phosphate buffer (pH 6.8) for duration of 24h. LBG-PVA Composite cryogel sample was taken followed by weighing of sample at several time intervals includes1, 2, 3, 4, 5, 6, 24 h respectively. After wards, wiping of sample with blotting paper was done for further investigating the weight gain [41]. The experiment was done in triplicate manner. However, percentage of swelling was determined by means of the formula described below:

$$\text{Swelling (\%)} = \frac{W_2 - W_1}{W_1} \text{ X } 100 \quad \ldots\ldots \quad (1)$$

Where W_1 is the initial weight of cryogel and W_2 is the final cryogel weight.

In vitro drug release

The formulated cryogel batches were investigated for estimating *in vitro* drug release behaviour of salbutamol sulphate by employing USP type II dissolution apparatus (TDT-08L, Electrolab, Mumbai India). A correctly weighed cryogel sample comprising salbutamol sulphate as active drug equivalent to 8 mg was placed in muslin cloth. The dissolution medium contained 900 ml of phosphate buffer having pH 6.8 was upheld at a temperature of (37±0.5) °C and stirred at 50 rpm. A 5 ml of sample was taken at several time intervals and replaced by fresh dissolution media of the same volume. The experiment was carried out in triplicate manner. The percentage release of the salbutamol sulphate in the dissolution media was estimated spectrophotometrically through determining absorbance at a wavelength of 276 nm.

RESULTS AND DISCUSSION

The blending of natural polymer with synthetic one is a beneficial technique for generating new material with improved modified properties. In the present research work, the composite cryogels comprising of two polymers loaded with drug i.e. salbutamol loaded LBG-PVA composite cryogel were successfully fabricated using freeze-thaw process as shown in fig. 1(a).

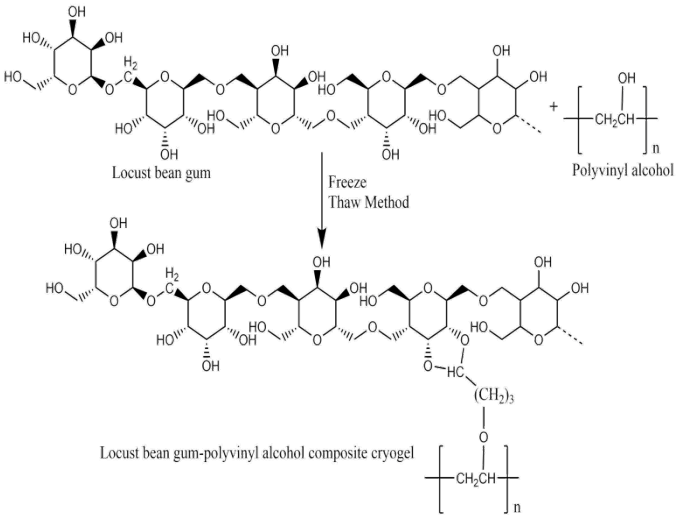


Fig. 1: Proposed scheme of LBG-PVA composite cryogel via freeze thaw process

Table 1: Influence of different factors on the percentage of salbutamol sulphate release from different batches of LBG-PVA composite cryogels formulated by means of two factor-three level factorial design

S. No.	Concentration of LBG(A)	Concentration of PVA(B)	*In vitro* drug release (%)	Swelling index (%)
1.	2 (-1)	5 (-1)	98.32±0.88	378±2.57
2.	2 (-1)	7.5 (0)	92.88±0.15	509±3.24
3.	2 (-1)	10 (+1)	72.66±0.75	534±2.33
4.	3.5 (0)	5 (-1)	90.5±0.23	460±4.47
5.	3.5 (0)	7.5 (0)	84.04±0.34	500±3.57
6.	3.5 (0)	10 (+1)	71.21±0.17	545±3.35
7.	5 (+1)	5 (-1)	88.71±0.36	499±0.19
8.	5 (+1)	7.5 (0)	75.84±0.54	567±4.54
9.	5 (+1)	10 (+1)	77.75±0.45	610±5.34
10.	3.5 (0)	7.5 (0)	85±0.52	525±2.46
11.	3.5 (0)	7.5 (0)	87.88±0.61	513±4.49
12.	3.5 (0)	7.5 (0)	83.33±0.56	487±5.81
13.	3.5 (0)	7.5 (0)	80.5±0.77	534±1.25

Data are expressed in mean±SD (n=3)

The technique of freezing and thawing was employed for proper cross linking of LBG-PVA. This physical method has been preferred due to its non-toxicity and good biocompatibility [42]. Also, the final product was creamish white in color with no odour.

Experimental design

The results of *in vitro* drug release rate and swelling index of formulations (each 24h) from different batches of LBG-PVA composite cryogels prepared, in accordance with the design protocol as demonstrated in table 1.

To determine the optimum amount of LBG and PVA for better *in vitro* drug release rate and swelling index, two factor-three level factorial design was applied. Total thirteen trial batches were formulated as per design protocol in accordance with two factors, i.e. amount of LBG (A) and amount of PVA (B) and studied on their effects *in vitro* release and swelling index. Average release (%) lies between 71.21% to 98.32%, whereas the swelling index (%) lies between 378 to 610 %. By employing the design expert software, polynomial equations were obtained by using the statistical factors such as sum of squares, degree of freedom, mean sum of squares and F value for analysis of the responses and analysis of variance (ANOVA). The obtained polynomial equations employing regression analysis for the responses (*in vitro* release and swelling index) are given below:

$$In\ vitro \text{ drug release } (\%) = +83.68 - 3.72 * A - 9.44 * B \ldots\ldots\ldots \quad (2)$$

$$\text{Swelling index } (\%) = +512 * 38 + 42.50 * A + 58.67 * B \ldots\ldots\ldots \quad (3)$$

In the above equations, the positive and negative symbols before the coefficients show their synergistic and antagonistic result respectively. The significance of models was considered on the basis of p-value and F-value.

Table 2: ANOVA analysis of polynomial model

	Model				Lack of fit	
Response factors	**R^2**	**Adjusted R^2**	**Predicted R^2**	**Adequate precision**	**F-value**	**p-value**
In vitro drug release (%)	0.7887	0.7465	0.5479	13.467	3.19	0.1409
Swelling index (%)	0.8636	0.8363	0.7484	18.887	1.66	0.3239

According to ANOVA analysis (table 2), it revealed that response surface model was significant (p-value<0.05) with 'lack-of-fit' non-significant (p-value>0.05). Significance of this model was further characterized by potentially high values of correlation coefficient (R^2) and adjusted correlation coefficient (adjusted R^2). Based on design data, reasonable agreement between adjusted $R^2$and Predicted R^2 was observed. With addition to this, adequate precision (>4) i.e. signal to noise ratio indicate that proposed model is suitable for navigating the design space. Also, large F-value shows that the effect of variance is greater than the error of variance. By analysing all parameters viz. optimum *in vitro* release (77.75%) with swelling index (610%), optimized batch to prepare desired composite cryogels was generated for further usage. The optimal parameters proposed to optimize the formulation were found to be 5% LBG and 10% PVA.

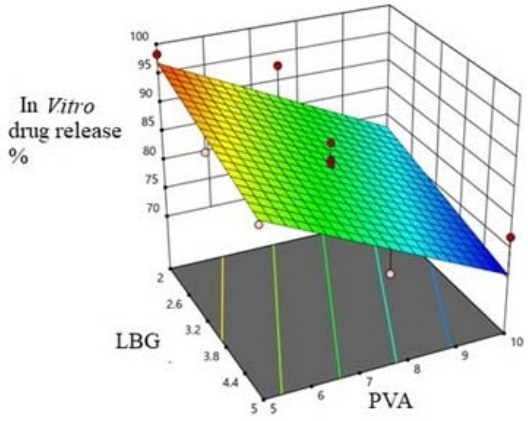


Fig. 2(a): Response surface plot displaying combined impact of concentrations of LBG and PVA on *in vitro* drug release (%)

Fig. 2(a) represent 3D response surface plot indicating the effect of different parameter on response surface variable. Three dimensional graphs clearly depict a linear relationship in which one factor attempts to favour the effect of another. Comparatively less LBG concentration with high PVA concentration can be ascribed to the required cryogel formation having elevated cross linking ability. The graph clearly depicts that increasing the concentration of LBG from 2% to 5%, percentage release of salbutamol gets increased while higher level of PVA polymer has more pronounced effect on the percentage release of drug. Hence, both the selected parameters were observed to influence the response variables. Similarly, in fig. 2(b), rise in concentration of PVA and LBG show linear relationship as it also denotes that, high concentration of LBG ultimately leads to increase in the swelling index (%). The network structure density besides swelling of the both polymers is accountable for the property of the swelling specifically demonstrated by composite cryogels. It is reported that swelling behaviour of hydrogels consist of continuous processes that are three in number, i.e. (a) imbibition of the cryogel network with solvent molecule, (b) relaxation of polymer chain and (c) elongation of cryogel network [43]. The involvement of LBG in the cryogels sturdily affects swelling behaviour so it was detected from both the plots that elevated LBG and PVA concentrations favour the cryogel with desired *in vitro* drug release and high swelling properties.

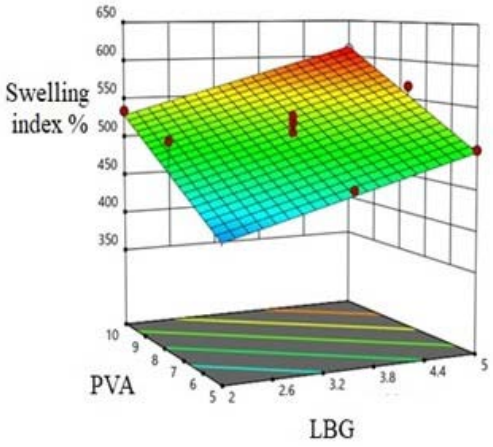


Fig. 2(b): Response surface plots displaying combined impact of concentrations of LBG and PVA on swelling index (%)

Fourier transform-infrared spectroscopy (FT-IR)

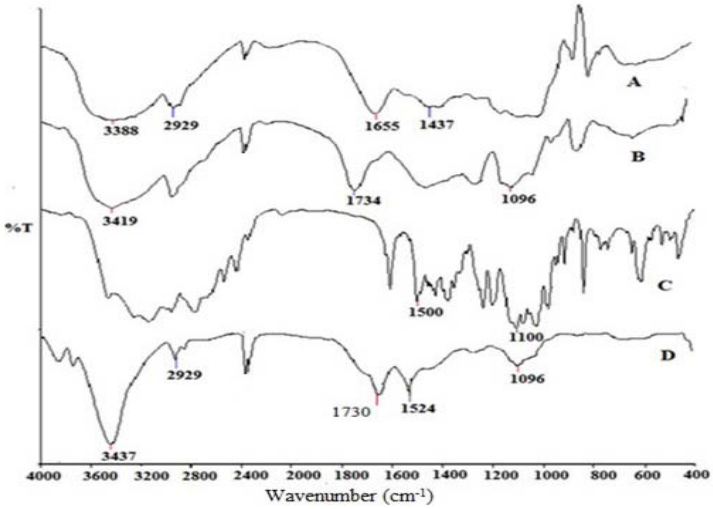


Fig. 3: FT-IR spectra of LBG (a), PVA (b), salbutamol sulphate (c) and LBG-PVA composite cryogel (d)

The FTIR technique is extensively employed for analyzing the functional groups. Fig. 3 displays the FTIR spectra of LBG, PVA, salbutamol sulphate, and LBG-PVA composite cryogels. The IR spectrum of LBG showed a broad peak at 3388 cm^{-1} is due to O-H stretching of hydroxyl group [44] and peak at 2929 cm^{-1} may be ascribed to stretching vibrations of–CH_2 [45]. The appearance of

peak at 1655 cm^{-1} is due to aryl-substituted of C=C. The broader peak ascribed at 1437 $cm^{-1}$is due to symmetrical stretching of carboxylate of LBG. The spectra of PVA shows a wide-ranging peak at 3419 cm^{-1} which can bedue to O-H stretching of free hydroxyl groups and characteristic peak at 2363 cm^{-1} is due to C-H stretching of alkanes. The characteristics peak at 1734 cm^{-1} assigned toC=O stretching of acetate of PVA where the broader peak at 1096 cm^{-1} signifies the bending of CH_2 group. The IR-spectrum of salbutamol sulphate showed sharp peaks at 1100 cm^{-1} (C-O stretching) and at 1500 cm^{-1} for O-H bending. Consequently, the augmentation of the O-H stretching band besides improving the intensity of C-H stretching along with their shifting to wave number in-between LBG combined with PVA reveals the occurrence of interaction among the PVA and LBG cryogels however the spectra of salbutamol loaded LBG-PVA composite cryogels shows sharp peak at 3437 cm^{-1} is due to O-H stretching of free hydroxyl groups.

Differential scanning calorimetry

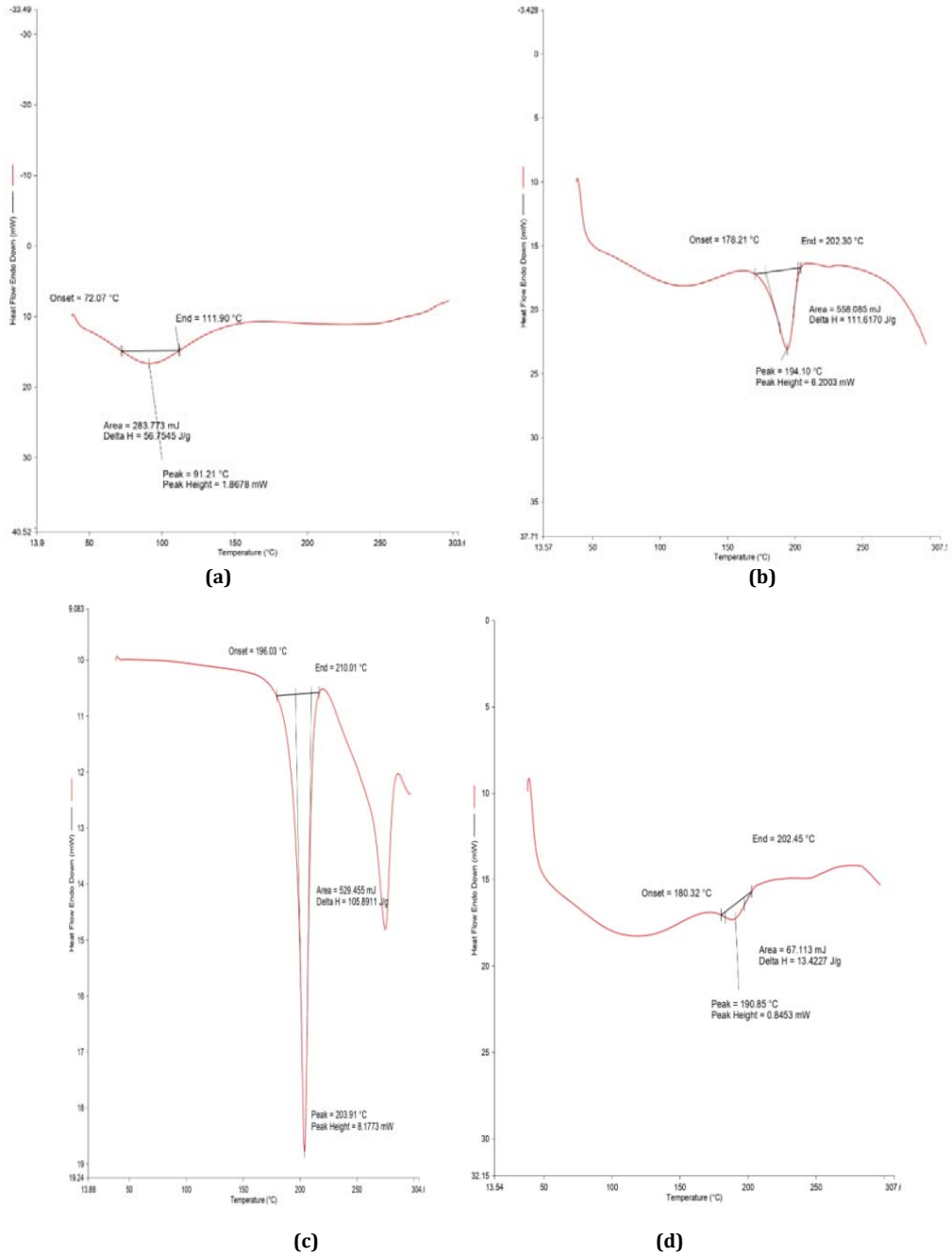


Fig. 4: (a) DSC thermogram of LBG(b) PVA (c) Salbutamol sulphate (d)LBG-PVA composite cryogel

Differential scanning calorimetry is an effective thermal analytical technique that determines change in heat capacity with temperature. Thermal analysis can be used for composite materials to determine the properties of the matrix material. With respect to the individual polymers, an increase in glass transition temperature is generally observed for the blend [46]. Fig. 4 represents the thermogram of LBG, PVA, salbutamol sulphate and LBG-PVA composite cryogels respectively. It can be observed from the DSC graph of LBG that broad endotherm at 91.21 °C with commencement at 72.07 °C and end at 111.90 °C with heat flow of 56.75J/g. This may be ascribed due to

evaporation of structural water present in natural polymer. Thermogram of PVA shows endothermic transitions commences at 178.28 °C with the peak at 194.10 °C and ends at 202.30 °C with the heat flow of 111.61J/g. The thermogram of salbutamol sulphate shows the endotherm at 203.91 °C with the onset of 196.08 °C and end at 210.91 °C with heat flow of 105.891J/g. Thermogram of LBG-PVA composite cryogels displays a broad endotherm with hump at 190.85 °C with commencement at 180.32 °C then finish at 202.32 °C having heat of flow that is 13.42J/g which suggests that modification has been taken place with change in thermal behaviour.

X-ray diffraction

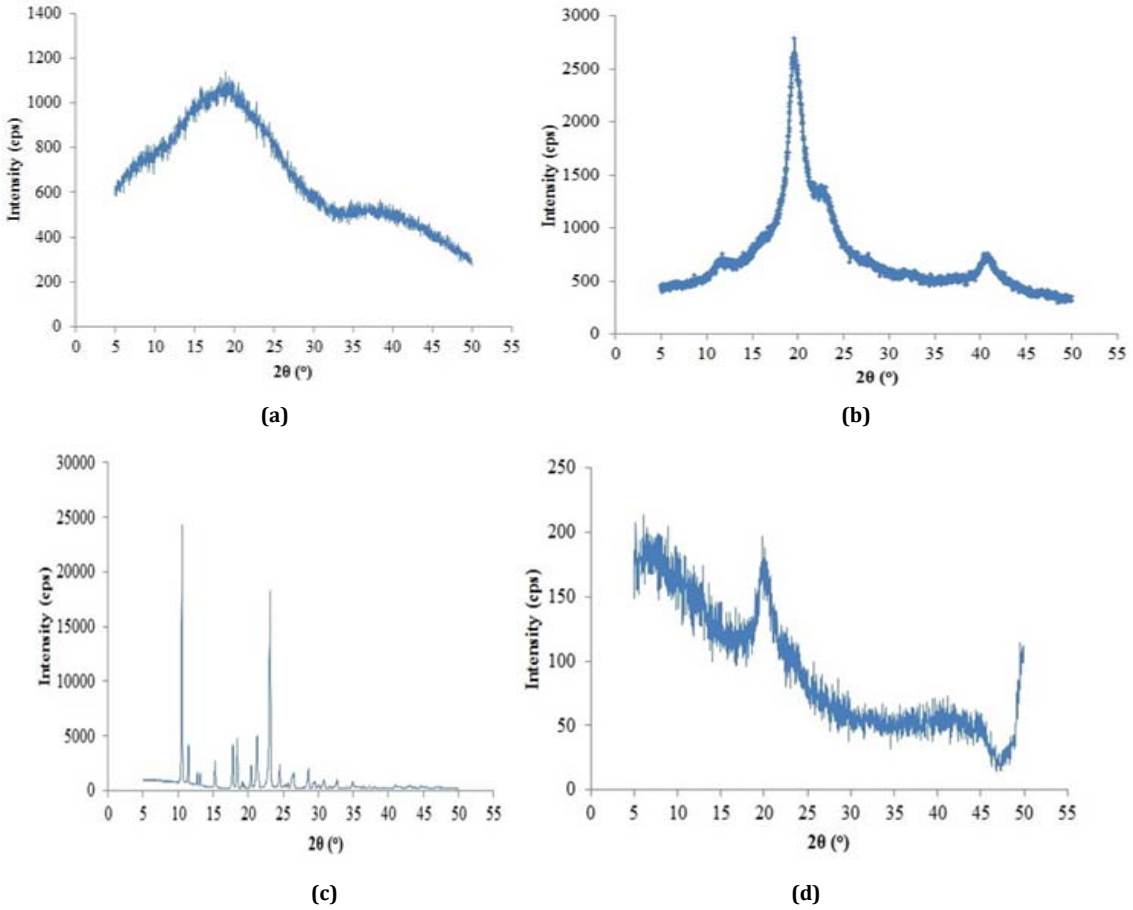


Fig. 5: XRD graph of LBG (a), PVA (b) Salbutamol sulphate(c) and LBG-PVA composite cryogel (d)

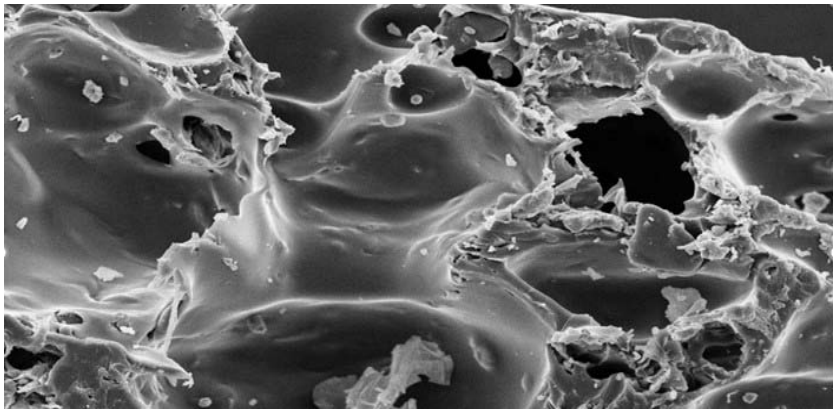
X-ray diffraction is a technique that is widely used to explore the nature of the polymer that whether it is crystalline or amorphous in nature. This technique is carried out to investigate the possible change in crystalline structure behaviour [47]. Fig. 5 demonstrating XRD pattern of optimized batch of LBG, PVA, salbutamol sulphate and LBG-PVA composite cryogel. Diffraction pattern of LBG clearly represent its amorphous behaviour with curve peak at 18.004°(2θ) while in pure PVA diffraction pattern, clear and sharp peak at 19.59°, 22.04°, 40.28°, (2θ) was observed which indicates that PVA is semi-crystalline in nature. Sharp and straight characteristic peaks at 10.56° and 21.22°, 23.11°, 28.53° (2θ) of salbutamol sulphate diffraction pattern clearly indicates crystalline nature of drug. However, diffraction pattern of LBG-PVA composite cryogel indicating characteristic peak at 19.83° (2θ) which suggest that formation of cryogels between two polymers contributes to a decrease in crystallinity [9].

Scanning electron microscopy

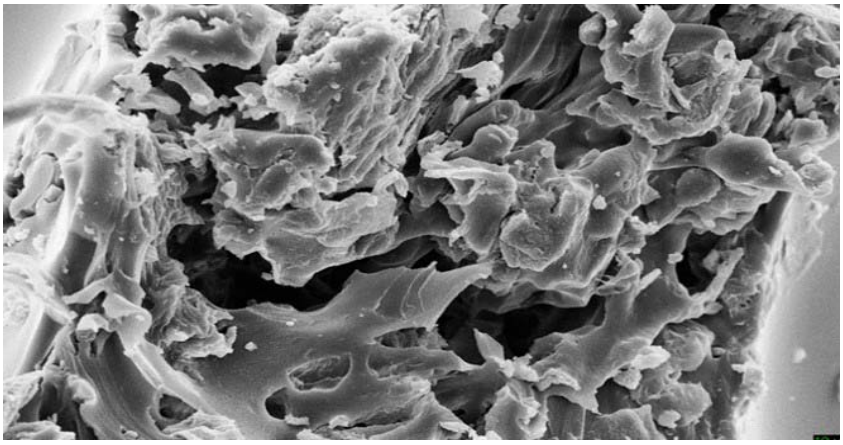
Scanning electron microscopy (SEM) is an electron optical imaging method that is widely employed in experiments for studying the size, morphology, porosity and shape of the hydrogel matrices. It is employed for determining surface topography, texture and particle size distribution [48]. The SEM images of LBG-PVA composite cryogel (fig. 6) showing the effects of freeze thaw cycle on polymer and drug loaded composite cryogels. Freeze thaw cycle not only ascertain the development of ice crystals on the amorphous region, forcing the polymer chains to be arranged in small ordered regions (crystallites) but also, such crystallites perform their function as physical cross links [49]. The porous structure of the hydrogel remains unaltered even after melting of ice crystals upon thawing. By this means, crystals serve as aporogen during the formation of hydrogel and with recurring freeze thaw cycle, size and number of crystallites get increased [50]. According to SEM image, LBG-PVA composite cryogels is porous in nature as interconnected and irregular pores with thick walls appear in the micrograph. Dominant role is played by pore connectivity in the rapid swelling of hydrogel. This interconnected pore structure facilitates the diffusion of the water molecules in and out which helps for further drug delivery [51].

Percentage of swelling

The swelling behaviour of the optimized batch of LBG-PVA composite cryogel in phosphate buffer pH6.8 for 24 h is depicted in the fig. 7. It can be seen, the swelling ability of the LBG-PVA cryogels increased considerably by taking both polymers in higher concentration. The cryogel having more pores swell more and tend to exhibit elevated water uptake capacity. Simultaneously, the complete hydrophilicity of the formedcryogel strongly influenced the swelling capability [52]. By increasing locust bean gum quantity, the cryogel networks became more hydrophilic consequently; more water was absorbed, leading to elevated swelling percentage.



(a)



b)

Fig. 6: Scanning electron micrograph of shape (a) and surface (b) of LBG-PVA composite cryogel

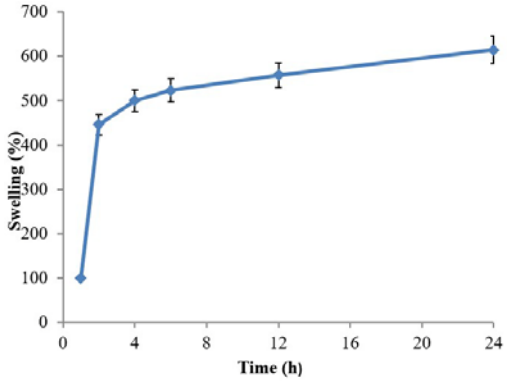


Fig. 7: Swelling (%) of optimized batch of LBG-PVA composite cryogel, values are given as mean; where n=3

In vitro release

Fig. 8 inferred the comparison of *in vitro* release behaviour of pure drug with its formulation i.e. salbutamol sulphate LBG-PVA composite cryogel. It can be observed from the plot (fig. 8) that composite cryogels could sustain the release of drug upto24 h (releases upto77.75±0.45%) while pure drug release completely in only 6h. For determining the kinetics in addition to mechanism of release of salbutamol sulphate from composite cryogels formulation, the data of release was subjected to fitting into several kinetic models. The $R^2$for zero-order, Higuchi square root kinetics, first-order, and korsemeyer–peppas models was found to be 0.947, 0.988, 0.799, 0.9270 respectively. Further the value of '*n*' the release exponent of korsemeyer–peppas model was determined to be (0.528). It was indicated from results that the salbutamol sulphate released from composite cryogels followed Higuchi square root of release kinetics with the release mechanism being the diffusion through the matrix.

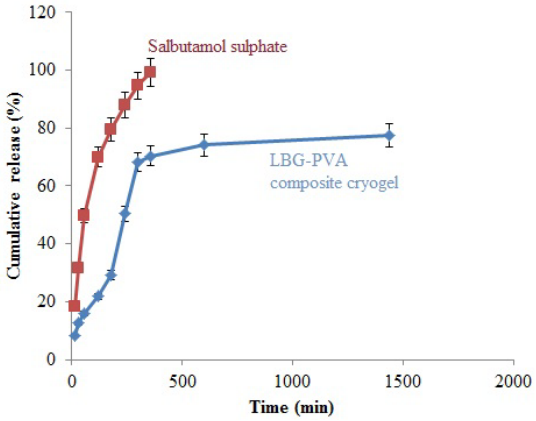


Fig. 8: *In vitro* release profile of optimized batch of LBG-PVA composite cryogel, values are given as mean; where n=3

CONCLUSION

The results obtained by optimization study inferred that the greater concentration of both LBG and PVA favoured release of salbutamol

sulphate in a sustained manner. The experimental findings display *in vitro* release of salbutamol sulphate as 77.75% over duration of 24 h following Higuchi's square root release kinetics. From experimental findings, it is revealed that, LBG-PVA composite cryogels could be utilized for fabricating a system for drug delivery in a sustained manner.

ACKNOWLEDGEMENT

The authors are thankful to Indian Institute of Technology, New Delhi for SEM analysis.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

There is no conflict of interest with reference to the publication of this paper.

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